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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,253	01/30/2006	Yukihiko Saeki	285327US0PCT	5754

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EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	**PAPER NUMBER**
1614	

NOTIFICATION DATE	DELIVERY MODE
09/12/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/566,253	SAEKI ET AL.	
	Examiner	Art Unit	
	Charleswort Rae	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,17-34* is/are pending in the application.

4a) Of the above claim(s) *2,3,5-12,17-28,30 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,29 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/28/06;1/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response with traverse (filed 6/25/07) to the Restriction/Election requirement, mailed 5/23/07, electing invention I, multiple myeloma as the disease species, and 2-benzyl-5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one as the compound species are acknowledged and made of record.

Applicant's statement divisional applications filed hereafter claiming the non-elected inventions should not be subject to double patenting ground of rejection is acknowledged.

Restriction/Election

Applicant's traversal arguments that a) inventions I-III are integrally linked as compounds, method of making and method of use apparently based on the assertion that the instantly claimed composition differs from the teaching of the cited reference (US Patent 6,348,468) with respect to the N-A-R3 side chain as A is a single bond when R3 is halogenated C1-6 alkyl group in the instant claimed invention, and b) a search of all the claims would not constitute a serious burden, are not found to be persuasive for the reasons previously made of record in the Office action mailed 5/23/07.

Status of the Claims

Claims 1-12, 17-34 are currently pending in this application.

Claims 13-16 are cancelled.

Claims 2-3, 5-12, 17-28, and 30-31 are withdrawn for examination purposes for being directed to non-elected subject matter.

Claims 1, 4, 29, and 32-34 are presented for examination.

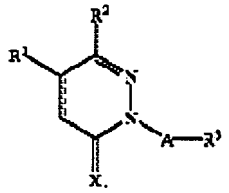
Claim rejections – 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

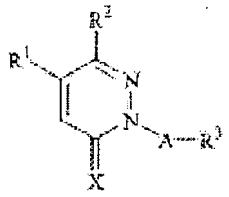
Claims 1, 4, 29, 32-33 are rejected under 35 USC 102(b) as being anticipated by Ohkuchi et al. (US Patent 6,348,468; **previously made of record in Restriction/Election requirement mailed 5/23/07**).

Ohkuchi et al. teach **2-benzyl-5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one** (see Example 132; col. 54) and methods of treatment comprising administering said compound, as representative of the below general formula:



wherein R^1 represents a (substituted) aryl group, R^2 represents a phenyl group substituted at 4-position by a lower alkoxyl group or a lower alkylthio group, R^3 represents a lower alkoxyl group, a halogenated lower alkyl group, a lower cycloalkyl group, a (substituted) aryl group, a (substituted) aryloxy group, a (substituted) nitrogen-containing heterocyclic ring residue, a (substituted) aminocarbonyl group or a lower alkylcarbonyl group, A represents a single bond, a lower alkylene group or a lower alkenylene group, X represents O or S, and the dashed line indicates that the carbon-carbon bond between the 4-position and the 5-position is a single bond or a double bond, or salts thereof; and also to medicines containing them as effective ingredients. These compounds have excellent inhibitory activity against interleukin-1β production, and are useful as preventives and therapeutics for immune system diseases, inflammatory diseases, ischemic diseases and the like.

Instant claims 4 and 32 are directed to a method of treatment and recite the identical compound, *2-benzyl-5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one.* Ohkuchi et al. teach a pharmaceutical composition comprising a pyridazine derivative of the above referenced formula or *salt thereof* and a pharmaceutically acceptable carrier (col. 3, lines 1-4). Instant claims 1, 4, 29, and 32, recite the term *"salt thereof."* Ohkuchi et al. teach that compounds having the above referenced formula are **effective ingredients** when administered orally or parenterally to an adult in an amount of about 0.01 to 1,000 mg per day (col. 13, lines 39-45); this reference teaching is construed to be the functional equivalent of the following term recited in instant claims 1 and 29: *"administering an effective amount of a pyridazine derivative represented by the below formula I*:



(I)

wherein:

R^1 means a phenyl or pyridyl group which may be substituted by 1 to 3 substituents selected from halogen atoms and C_{1-4} alkoxy groups;

R^2 means a phenyl group which may be substituted at the 4-position thereof with a C_{1-4} alkoxy group or C_{1-4} alkoxythio group and may also be substituted at one or two other

positions thereof a like number of substituents selected from halogen atoms, C_{1-6} alkoxy groups and C_{1-6} alkoxythio groups;

R^1 means a hydrogen atom; a C_{1-6} alkoxy group; a halogenated C_{1-6} alkyl group; a C_{3-6} cycloalkyl group; a phenyl, pyridyl or phenyloxy group which may be substituted by 1 to 3 substituents selected from halogen atoms, C_{1-6} alkyl groups, C_{1-6} alkoxy groups, carboxyl groups, C_{2-7} alkoxycarbonyl groups, nitro groups, amino groups, C_{1-6} alkylamino groups and C_{1-6} alkylthio groups; a substituted or unsubstituted piperidino, piperidyl, piperazino or morpholino group; a substituted or unsubstituted aminocarbonyl group; a C_{2-7} alkylcarbonyl groups; or a substituted or unsubstituted piperazinocarbonyl group;

A means a single bond, a C_{1-6} linear or branched alkylene group, or a C_{2-6} linear or branched alkenylene group; and

X means an oxygen atom or a sulfur atom, with a proviso that A is a single bond when R^3 is a halogenated C_{1-6} alkyl group.

Ohkuchi et al. teach *ischemic nephritis* (col. 13, lines 10-23), which is reasonably construed to exemplify the term *"a kidney disease,"* as recited in instant claim 33. The term *"inhibiting OPN production"* as recited in instant claim 1, is construed to be an inherent characteristic of the instantly claimed pyridazine compounds; while the term *"a disease resulting from enhanced OPN production"* as recited in claim 29 is satisfied in view of instant claim 33 which recites the term *"a kidney disease."* See above discussion of the term "a kidney disease."

Thus, claims 1,4, 29, 32-33 are rejected as being anticipated by Ohkuchi et al. for the above reasons.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 34 is rejected under 103(a) as being unpatentable over Ohkuchi et al. (US Patent 6,348,468), in view of McPhaden et al. Plasma osteopontin levels in multiple myeloma. Blood. 1994;84 (10, Suppl 1), page 177a, abstract #674).

The discussion of Ohkuchi et al. in connection with the rejection under 102(b) is incorporated by reference. Although Ohkuchi et al. teach pyridazine derivatives that have excellent inhibitory activity against interleukin-1β production which are useful as

medicines for the prevention and treatment of diseases caused by stimulation of interleukin-1β production e.g. immune system diseases, inflammatory disease, ischemic diseases, osteoporosis and the like (col. 13, lines 10-23), they do not teach multiple myeloma.

McPhaden et al. teach osteopontin (OPN) appears to be important in bone metabolism and may be a clinical marker of osteoblast and/or osteoclast activity in multiple myeloma (abstract). McPhaden et al. also teach that a number of osteoclast activating factors have been implicated in multiple myeloma including interleukin-1β (IL-1β).

Based on the teaching of McPhaden et al., someone of skill in the art would have been motivated to combine the teachings of Ohkuchi et al. and McPhaden et al. to create the instant inventive concept. Thus, someone of skill in the art at the time the instant claimed invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Claim rejections – 35 USC 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 USC 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 29, and 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 29 recite the limitation *"A means a single bond, a C1-6 linear or branched alkylene group, or a C2-9 linear or branched alkenylene group."* It is not clear what the term *"a single bond"* specifically refers to. For instance it is not clear whether the *" single bond"* refers to the attachment of the R^3 substitutent recited in instant claim 1, for example, or the bond that connects A to the Nitrogen-containing ring.

Further, the recitation of the term *"X means an oxygen atom or a sulfur atom, with the proviso that A is a single bond when R^3 is a halogenated C1-6 alkyl group"* further confuses the meaning of A in view of the fact that A may be a single bond even when R^3 is an unsubstituted phenyl group (as exemplified by then structure of *2-benzyl-5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one).*

Alternatively, instant claims 1 and 29 are indefinite because they not provide proper antecedent basis for claims 4 and 32 wherein R^3 is unsubstituted phenyl

Claims 1 and 29 are rejected under 112, second paragraph, on different grounds for failing to recite essential subject matter necessary for someone of skill in the art to practice the invention as claimed. Specifically, claims 1 and 29 fail to recite a host/subject/patient to whom the effective amount of the pyridazine derivative will be administered.

Dependent claims 4, 32, 33, and 34 are rejected for being dependent on a rejected claim.

Claims 1 and 29 recite the term "OPN" but fails to state the full meaning of the term at the first occurrence the term is recited in the claim. This limitation is vague and indefinite because it is not clear what "OPN" means. It is suggested that this specific

rejection may be overcome by either replacing the term "OPN" with the full name or, alternatively, amend the claim by inserting the full name in parenthesis at the first occurrence of the term "OPN" in the claim.

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4, 29, and 32-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-9 of copending US Patent Application No, 11/574,319. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims.

In particular, reference claim 1 is generally directed to a method for the prevention and/or treatment of rheumatoid arthritis in a subject comprising administering a composition comprising 2-benzyl-5(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one (i.e. the identical compound species recited in instant claim 4) and methotrexate. The recitation of the term "prevention .. of rheumatoid arthritis in a subject" reasonably encompasses treatment of subjects with or without arthritis e.g. multiple myeloma. Thus, claims 1, 4, 29, and 32-34 are deemed to be anticipated by Appl. '319.

For the same reasons stated above, claims 1, 4, 29, 32-34 are similarly deemed to be anticipated by Ohkuchi et al. (US Patent 6,348,468). The discussion of Ohkuchi et al. in connection with the above rejection under 102(b) is incorporated by reference. Thus, claims 1, 4, 29, and 32-34 are rejected on the ground of nonstatutory obviousness-type double patenting.

Relevant Art of Record

The below art references made of record and relied upon is considered pertinent to applicant's invention.

Chabas et al. (US Patent Application Publication No. 2005/0119204 A1) teach a methods for inhibiting the onset of, and treating, osteopontin-related disorders, as well as compositions for practicing the same (page 9, para.0137 to page 16, para. 0191; see also abstract).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.'

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the

automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

28 August 2007
CER

BRIAN-YONG S. KWON
PRIMARY EXAMINER